

### REMARKS

Claims 1-4, 7, 9-21, 57 and 58, and 61-63 are pending. Claim 11 has been canceled. Claims 1 and 7 have been amended. New claim 64 has been added. In the Office Action dated June 11, 2006, claims 1-4, 7, 9-21, 57-58, and 61-63 were rejected under 35 U.S.C. § 112 ¶ 2 as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Claims 1-4, 9-16, 18-21, 57-58, and 61-62 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,398,956 to Coville et al. (“’956 Patent”) in view of U.S. Patent No. 4,695,430 to Coville et al. (“’430 Patent”). Claim 7 was rejected under 35 U.S.C. § 103(a) as being unpatentable over the ‘956 Patent and the ‘430 Patent, and in further view of U.S. Patent No. 6,446,516 to Sullivan (“Sullivan”). Claim 17 was rejected under 35 U.S.C. § 103(a) as being unpatentable over the ‘956 Patent and the ‘430 Patent, and in further view of U.S. Patent No. 5,043,590 to Strandberg, Jr. et al. (“Strandberg”). Claim 63 was rejected under 35 U.S.C. § 103(a) as being unpatentable over the ‘956 Patent and the ‘430 Patent, and in further view of U.S. Patent Publication No. 2001/0052460 A1 to Chien et al. (“Chien”).

#### Rejections Under 35 U.S.C. § 112 ¶ 2

Claims 1 and 61 are rejected under 35 U.S.C. § 112 ¶ 2 as being indefinite for reciting a seal positioned between an inlet and a reservoir. Applicants respectfully assert that the claim term is not indefinite. A seal may be placed between adjoining structures, even where fluid flow occurs between them in order to prevent fluid from leaking out at the interface between the two adjoined structures. Seals such as O-rings and gaskets are often used to secure structures to one another in manner allowing fluid flow between them.

In the present case claim 1 recites “at least one area of fluidic communication between one of said plurality of outlets and one of said inlets,” which clarifies that there is a fluid passageway formed at one or more locations on the seal.” Claim 61 likewise recites “a seal positioned between the fluid manifold base and the microfluidic chip, the seal defining at least one area of fluidic communication between one of said reservoirs and one of said inlets.” The claims therefore make clear that the seal includes a specific area that allows for fluid communication.

Claim 11 is rejected under 35 U.S.C. § 112 ¶ 2 as being indefinite for reciting the claim limitation “low dispersion.” By this paper, claim 11 has been canceled rendering its rejection moot.

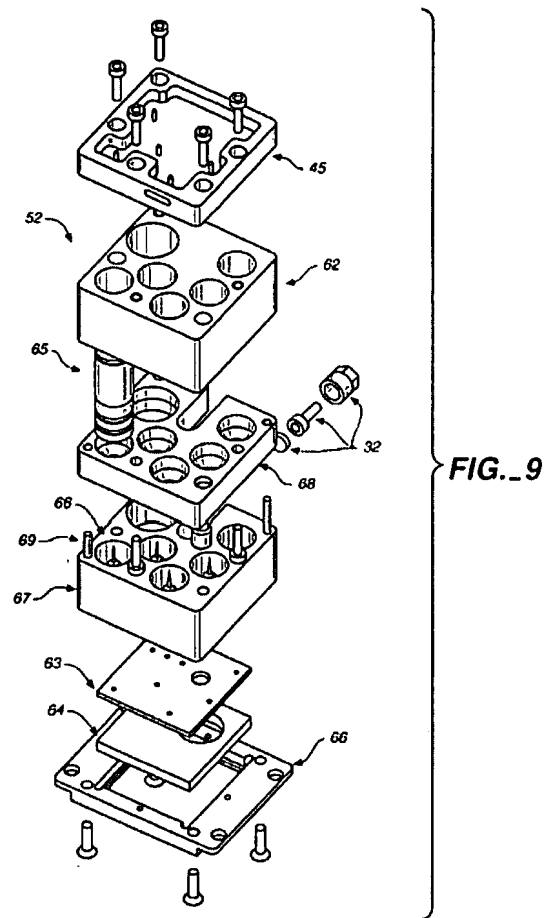
### Discussion of the Disclosed Embodiments

The disclosed embodiments of the invention will now be discussed in comparison to the prior art. Of course, the discussion of the disclosed embodiments, and the discussion of the differences between the disclosed embodiments and the prior art subject matter, do not define the scope or interpretation of any of the claims. Instead, such discussed differences merely help the Examiner appreciate important claim distinctions discussed thereafter.

In some embodiments, an apparatus for separating sample and detecting target analytes includes a reservoir base (e.g. 67; See Figure 9 at right) defining a number of bays within which one or more reservoirs (65) are mounted. The reservoir base mounts to a microfluidic chip (63) having a number of channels and chambers embedded therein between the upper and lower surfaces of the chip. Inlets extend through the upper surface of the chip to permit fluid to enter the chip from the reservoirs. The inlets are arranged to align with outlets formed in the reservoir base. The outlets in the reservoir base are each in fluid communication with reservoirs mounted within the reservoir base.

The inlets are in fluid communication with a sample introduction port and a separation channel embedded within the chip. The microfluidic chip may include a separation channel having a circuitous or serpentine shape. Fluids from the reservoir move through the separation channel by means of electroosmotic flow such that components of the fluid are separated. A detector positioned within the microfluidic chip interrogates the fluid within the separation channel by, for example, exposing the fluid to light and observing, for example, any fluorescence that occurs.

One or more of the reservoirs may couple to a power source to facilitate electroosmotic flow. The reservoir may include two chambers with one connected to the power source and the other containing a fluid. The microfluidic chip may likewise be coupled to a



**FIG. 9**

power source such that the change in electrical potential between itself and the reservoir urges fluid from the reservoir to flow through the chip.

#### Discussion of the Cited References

The '956 patent discloses a filtration cell in which a piercing instrument (16) and a reservoir (12) mount to a support (14). The support is mounted to a base (20) having an outlet port (22) formed therein. A membrane (18) is positioned between the outlet port (22) and the support (14). A cross flow over the membrane is induced by creating a low pressure in the reservoir (12) such that fluid is drawn from a container (26) placed over the piercing instrument. A portion of the fluid is allowed to permeate the membrane (18) and flow out the outlet port (22).

The '956 patent does not mention a microfluidic chip or suggest how a detector could be incorporated therein. The '956 patent further fails to disclose any of the fluid handling structures formed in the microfluidic chip of the disclosed embodiment. For example, the '956 patent does not disclose a reservoir base for receiving reservoirs and having a plurality of outlets each aligned with an inlet extending through an upper surface of a microfluidic chip. The '956 patent only discloses a membrane (18) positioned between a support (14) and a base (20) with openings formed only in the base (20). There are, for example, not a plurality of outlets on the support (14) aligned with a plurality of inlets on the membrane (18) or base (14). There is, further, no separation channel encapsulated between upper and lower surfaces of the membrane (18), but rather only open grooves that are formed on the outer surfaces of the membrane itself. There is, further, no seal positioned between the support (14) and the membrane (18). The support (14) is secured only to the base (20), leaving only open space between the membrane (18) and the support (14).

The '430 patent discloses an analytic apparatus in which fluid samples are encapsulated within cells. The cells are then processed by heating them and examining them optically. The portion of the fluid being analyzed remains at all times within the cell. The '430 patent likewise fails to disclose a microfluidic chip and the fluid handling structures formed therein in the disclosed embodiment. The '430 patent further fails to teach a reservoir having two chambers wherein one is coupled to a power source. The '430 patent teaches that blood is tested by inserting two electrodes and measuring the conductivity of the blood. Col. 1, Ins. 50-63. However, the cited passage does not mention a reservoir having two chambers nor does it

mention that the reservoir is disposed in an apparatus as in the disclosed embodiment. As mentioned previously, the '430 patent teaches only the processing of fluid within discrete cells and does not disclose the fluid handling apparatus of the disclosed embodiment.

There is no teaching or suggestion to combine the '430 patent, which deals only with discrete cells, with the '956 patent, which is a simple filtration cell that provides no indication that a detector could be mounted thereto as described in the disclosed embodiment. Inasmuch as neither reference discloses a separation channel, neither reference teaches or suggests mounting a detector such that it can interrogate a separation channel. The '956 patent teaches only that fluid separated using the membrane (18) may be drained through the outlet (22). The '956 patent does not teach that detection occurs in a separation channel within the microfiltration cell.

Chien fails to remedy the deficiencies of the '430 and '956 patents. Chien discloses a pressure transmission system for controlling the pressure of fluid injected into a microfluidic chip. Abstract. Chien discloses only the use of pressure to control fluid flow and does not discuss electroosmotic flow as disclosed by Applicants. Chien, further, therefore does not teach coupling a two-chambered reservoir to a power source to control electroosmotic flow.

Chien discloses a microfluidic device but fails to disclose the reservoir base disclosed by Applicants, nor does Chien disclose mounting a reservoir base to a microfluidic chip in the manner disclosed by Applicants. Chien further fails to disclose a microfluidic chip having inlets, sample introduction ports, and separation channel as disclosed by Applicants.

#### Discussion of the Claims

Turning now to the claims, the differences between the cited references and the claimed invention will be particularly pointed out.

With respect to claim 1, none of the cited references, whether alone or in combination, teach all of the limitations of the claim, including “a fluid manifold base defining a plurality of bays and a plurality of outlets, each outlet extending between one of the plurality of bays and a lower surface of the fluid manifold base; and a plurality of reservoirs coupled to the fluid manifold base, each positioned within one of the plurality of bays” and “a microfluidic chip comprising: a planar upper surface and a lower surface; a plurality of inlets piercing the upper surface, the inlets positioned in locations corresponding to the plurality of outlets of the fluid manifold base and each in fluid communication with one of the plurality of outlets; and a

separation channel embedded within the microfluidic chip between the upper and lower surfaces thereof, the separation channel in fluid communication with at least one of said inlets; a sample introduction port embedded within the microfluidic chip between the upper and lower surfaces thereof, the sample introduction port in fluid communication with said reservoir module and at least one of the plurality of inlets; a seal positioned between the fluid manifold base and the microfluidic chip, the seal defining at least one area of fluidic communication between one of said plurality of outlets and one of said inlets; a detection module positioned to interrogate at least a portion of the separation channel.” (emphasis added).

With respect to claim 7, as noted by the Examiner, none of the cited references disclose an apparatus “wherein at least one of said plurality of reservoirs comprise at least two chambers, wherein one of the at least two chambers is in fluidic communication with at least one of said plurality of inlets, and the second of said at least two chambers is in electrical communication with the power module.” Claim 7 has been amended to incorporate the limitations of claim 1 and is now in condition for allowance.

With respect to claim 61, none of the cited references, whether alone or in combination, teach or suggest all of the limitations of the claim, including “a microfluidic chip having upper and lower surfaces, the upper surface being in contact with the fluid manifold base, the microfluidic chip comprising: a plurality of inlets piercing the upper surface and positioned in correspondence with the plurality of reservoirs; and a separation channel embedded within the microfluidic chip between the upper and lower surfaces, the separation channel being in fluid communication with at least one of said inlets; and a seal positioned between the fluid manifold base and the microfluidic chip, the seal defining at least one area of fluidic communication between one of said reservoirs and one of said inlets; a detection module positioned to interrogate at least a portion of the separation channel.” (emphasis added).

All of the claims remaining in the application are now clearly allowable.  
Favorable consideration and a timely Notice of Allowance are earnestly solicited.

Respectfully submitted,

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